



Original Research Article

Minimal Hepatic Encephalopathy- The Invisible Challenge!

Authors

Dr Madhu P. Bansode¹, Dr Pankaj H. Bansode², Dr Rakesh Patil³

¹Associate Professor, Bharati Vidyapeeth (Deemed to be University) Medical College, Pune

²Associate Professor in Surgery, Bharati Vidyapeeth (Deemed to be University) Medical College, Pune

³Resident in Medicine, Bharati Vidyapeeth (Deemed to be University) Medical College, Pune

Corresponding Author

Dr Pankaj H Bansode

Associate Professor in Surgery, Bharati Vidyapeeth (Deemed to be University) Medical College, Pune

Abstract

Minimal hepatic encephalopathy (MHE) is the earliest form of hepatic encephalopathy and can affect up to 80% of cirrhotic patients. MHE patients have normal mental and neurological status on standard clinical examination but exhibit a number of neuropsychiatric and neurophysiological defects, thus causing difficulty in daily tasks including driving etc.

Aim and objective of study: *There are few studies conducted in India related to MHE. Hence the present study was undertaken to determine the prevalence of Minimal Hepatic Encephalopathy.*

Material and Methods: *50 adult patients with established liver cirrhosis were studied for neuropsychiatric and neurophysiologic tests.*

Results: *The prevalence of Minimal Hepatic encephalopathy (MHE) was 30% in the study population.*

Conclusions: *MHE is an significant disorder that may seriously impair patients' daily functioning and quality of life. MHE predicts the development of overt hepatic encephalopathy. In spite of the various tools used, in the absence of a "gold standard," a combination of test methods is recommended to diagnose MHE most reliably. The key point of emphasis is to identify the patients in presymptomatic stage and intervene early enough in order to halt the morbid and fatal future outcomes in liver cirrhotic patients.*

Keywords: *MHE (minimal hepatic encephalopathy), neurophysiological and neuropsychiatric tests.*

Introduction

Hepatic encephalopathy (HE) is often a critical sequel of chronic liver disease with significant morbidity, mortality and healthcare costs.

Minimal hepatic encephalopathy (MHE) is the earliest form of hepatic encephalopathy and can affect up to 80% of cirrhotic patients. It is associated with poor outcomes, with reportedly decreased survival rates after even the first

episode of HE (hepatic encephalopathy).¹ HE can be graded by severity using the West Haven Criteria and can be divided into minimal HE (MHE) and overt HE (OHE). Minimal hepatic encephalopathy is not only associated with poor prognosis but also significant detrimental effects to quality of life and a substantial burden to caregivers and healthcare systems.

Definition of Minimal Hepatic encephalopathy (MHE).

MHE is condition in which patients with liver cirrhosis have normal mental and neurological status on standard clinical examination but exhibit a number of neuropsychiatric and neurophysiological defects. MHE is present in 25-85% of cirrhotic patients without overt hepatic encephalopathy.

MHE is also defined as patients with abnormal psychometrics test without meeting criteria for OHE. Psychometric Hepatic Encephalopathy Score (PHES) has been shown to be specific and sensitive in determining MHE.² PHES is composed of five tests: number connection test-A, number connection test-B, serial dotting test, line tracing test, and digit symbol test. Several computerized tests have also aided in the diagnosis of MHE. Inhibitory control testing uses letters projected on the screen to test if patients can respond only to certain letters. Patients with MHE tend to have longer reaction times, high rates of inappropriate reactions and lower rates of appropriate reactions. The inhibitory control test has a sensitive of 87% and specificity of 77%.³

There are very few studies conducted in India related to MHE. Hence the present study was undertaken to evaluate MHE in liver cirrhotic disease patients.

MHE has been diagnosed in patients with liver cirrhosis and also in patients with noncirrhotic portal hypertension. The prevalence of MHE has been reported in as many as 20%–84% of cirrhotics, depending on which methods or tools are used and fixed diagnostic cut-offs.^{4,5}

Large variations in the prevalence of MHE are related to prior episode of OHE, severity of liver disease, age, presence of esophageal varices, and surgical portosystemic shunts. Patients who develop MHE are older, more often have alcohol as etiology of cirrhosis, have history of overt HE in the past, have more severe liver disease, and more often have esophageal gastric varices.^{4,5}

Clinical Characteristics

Patients with MHE have a normal neurological examination; however they may still be symptomatic. Symptoms relate to disturbances in sleep, memory, attention, concentration and other areas of cognition.^{8,9} A higher frequency of sleep disturbance in cirrhotic patients with MHE has been confirmed in studies using HRQOL (health related quality of life) questionnaires.^{8,9} Sleep disturbance in cirrhosis is not associated with cognitive impairment; thus it may not truly be an MHE symptom. Defective memory may be a sign of MHE.⁷ This impairment is predominantly related to deficits in attention and visual perception. Memory deficit of MHE seems to comprise short-term but not long-term memory impairment. This can be described as an encoding defect, in which memory recall (or retrieval) is intact.

Diagnosis of MHE

The absence of hepatic encephalopathy clinically is key to the suspicion of MHE and can only be diagnosed reliably by a detailed patient history and a comprehensive neurological assessment of consciousness, cognitive, and motor function.

Various tools have been evaluated for the diagnosis of MHE and include neuropsychological, neurophysiological tests, and computerized tests. Regional cerebral blood flow changes,¹¹ and magnetic resonance imaging and spectroscopy,¹² though useful for understanding pathogenic mechanisms, are currently not considered of diagnostic value.

Critical flicker frequency (CFF) tests the ability of a patient to perceive flickering and its fusion threshold. The CFF threshold measures visual discrimination and general arousal.¹⁴ CFF is a simple, reliable and accurate method for the diagnosis of MHE. The technique shows little dependence on age, education or training.¹³ Inhibitory control test (ICT) is a computerized test of attention and response inhibition. MR imaging techniques complement neuropsychological evaluation of MHE.¹⁰

Diagnostic Criteria for MHE

The diagnostic criteria for MHE have not been standardized but rest on careful patient history and physical examination, normal mental status examination, demonstration of abnormalities in cognition and/or neurophysiological function, and exclusion of concomitant neurological disorders.

Survival

Current data suggest that patients with MHE tend to have more frequent episodes of overt HE and poorer survival than in those without MHE, and indicate that patients with MHE have a more advanced liver disease. A high Child - Turcotte - Pugh score and PHES (psychometric hepatic encephalopathy score) were associated with a poor prognosis.

Treatment

Standard Pharmacological therapy with lactulose and lactitol, L-ornithine– L-aspartate (doubtful value) is recommended by experts.

Aim and Objective

To determine the prevalence of Minimal Hepatic Encephalopathy and to study the various

parameters (variables) of MHE in patients with liver disease.

Material and Methods

Type of study: This was observational cross-sectional study.

Sample size: 50 patients from outpatient & inpatients of a tertiary care center were included in the study. After ethical clearance and informed consent, patients underwent detailed history recording, clinical examination along with relevant laboratory investigations and clinical tests.

Inclusion criteria: All adult patients with liver disease aged above 20 years with established liver cirrhosis without hepatic encephalopathy were included in study.

Exclusion criteria: All types of encephalopathies such as Hepatic, Uremic, Hypertensive, Septic, Hypoxic, Metabolic, Malarial etc and all psychiatric patients.

After standard routine investigations, following special investigations were done:

Psychometric testing-

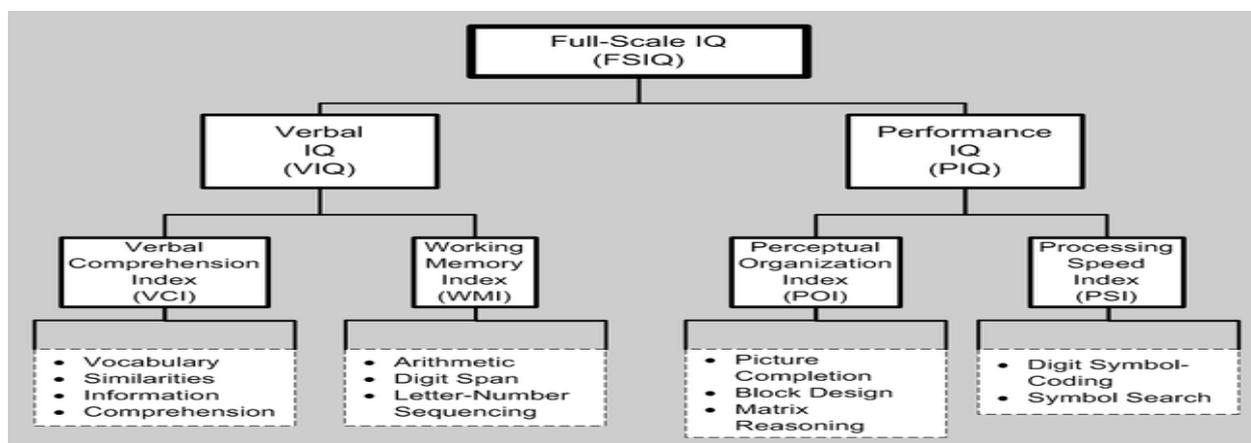


Fig no 1: Wechsler Adult intelligence scale

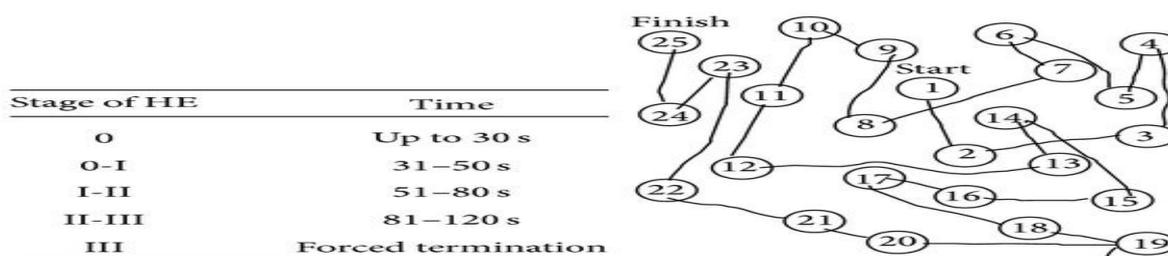


Fig no 2: Number connection test

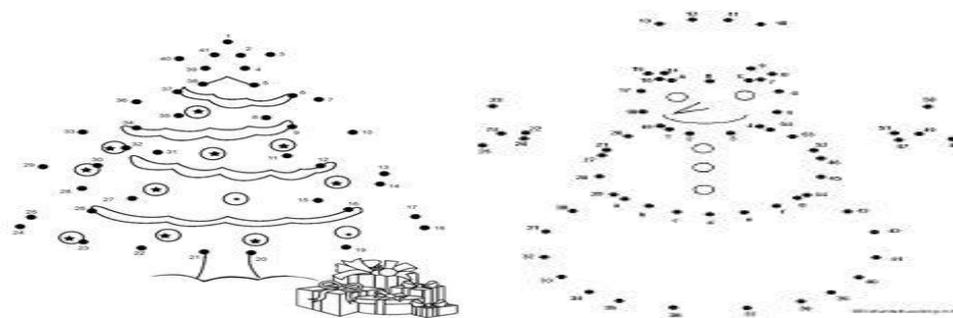
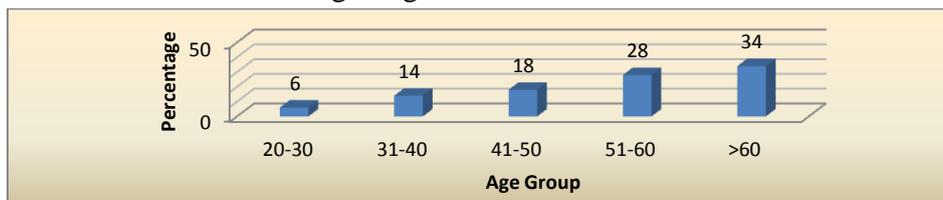


Fig no 3: Picture completion test

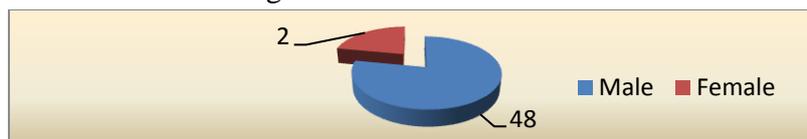
Observations and Results

Figure 1: Distribution of Patients according to age-



Majority patients were >60 years (34%) followed by age 51-60 years (28%)

Figure 2: Distribution of Patients according to sex:



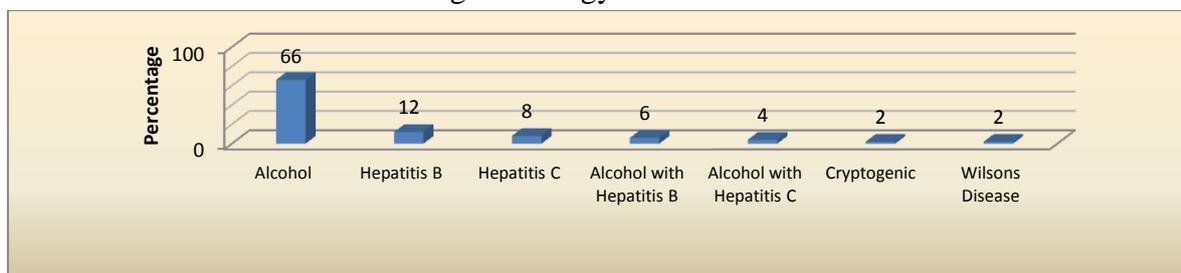
Out of 50 patients 48 patients (96%) were males and 2 (4%) were females.

Figure 3 -Patients according to prevalence of Minimal Hepatic encephalopathy:



The prevalence of Minimal Hepatic encephalopathy (MHE) was 30% among the study population.

Figure 4: Distribution of Patients according to etiology of MHE:



The main etiology among patients of minimal hepatic encephalopathy was alcohol (66%) followed by Hepatitis B infection (12%). The Hepatitis C infection was observed in 8% patients. The Wilson disease was observed in 2% patients.

Summary

The present study undertaken to study prevalence of Minimal Hepatic Encephalopathy in liver disease revealed the following points:

- Majority of patients were in age group >60 years (34%) followed by age group 51-60 years (28%)

- The mean age among patients was 52.44 ± 12.79 years.
- Out of 50 patients 48(96%) were males and 2(4%) were females.
- The prevalence of Minimal Hepatic encephalopathy (MHE) was 30% among the study population.
- The main etiology of minimal hepatic encephalopathy among study population was alcohol (66%) followed by Hepatitis B infection (12%). Hepatitis C infection was observed in 8% patients. Wilson disease was observed in 2% patients.

Conclusions

Minimal hepatic encephalopathy (MHE) has neurophysiological defects and its prevalence is variable in cirrhotics. In the present study its prevalence is 30%. It is characterized by a specific, complex cognitive dysfunction which is independent of sleep dysfunction or problems with overall intelligence. MHE is an important disorder that may seriously impair patients' daily functioning and quality of life. MHE may predict the development of overt hepatic encephalopathy. Various tools have been evaluated for the correct diagnosis of MHE, however, in the absence of a "gold standard," combination of test methods is recommended to diagnose MHE most reliably. The key point of emphasis is to identify the patients in presymptomatic stage and intervene early enough before the downhill spiraling course in disease progression spells an impending doom.

References

1. Stinton LM, Jayakumar S. Minimal hepatic encephalopathy. *Canadian Journal of Gastroenterology*. 2013;27(10):572-574
2. Bajaj JS, Wade JB, Sanyal AJ. Spectrum of neurocognitive impairment in cirrhosis: implications for the assessment of hepatic encephalopathy. *Hepatology* 2009;50: 2014-2021.
3. Mardini H, Saxby BK, Record CO. Computerized psychometric testing in minimal encephalopathy and modulation by nitrogen challenge and liver transplant. *Gastroenterology* 2008;135:1582-1590.
4. Bajaj JS, Heuman DM, Sterling RK, et al. Validation of encephalapp , smartphone-based stroop test, for the diagnosis of overt hepatic encephalopathy. *Clin Gastroenterol Hepatol* 2015;13:1828-1835.e1.
5. Tan HH, Lee GH, Thia KTJ, Ng HS, Chow WC, Lui HF. Minimal hepatic encephalopathy runs a fluctuating course: results from a three-year prospective cohort follow-up study. *Singapore Med J* 2009; 50(3): 255-260
6. Cordoba J, Cabrera J, Lataif L, Pener P, Zee P, Blei AT. High prevalence of sleep disturbances in cirrhosis. *Hepatology* 1998; 27: 339-45.
7. Weissenborn K, Heidenreich S, Gieweke-meyer K, Ruckert N, Hecker H. Memory function in early hepatic encephalopathy. *J.Hepatol*.2003;39: 320-5.
8. Prasad S, Dhiman RK, Duseja A, Chawla YK, Sharma A, Agarwal R. Lactulose improves cognitive functions and health-related quality of life in patients with cirrhosis who have minimal hepatic encephalopathy. *Hepatology* 2007; 45: 549-59.
9. Goeneweg M, Moerland W, Quero JC. Screening of subclinical hepatic encephalopathy. *J. Hepatology* 2000; 32: 748-53.
10. Bajaj JS, Hafeezullah M, Hoffmann RG et al. Navigation skill impairment: Another dimension of the driving difficulties in minimal hepatic encephalopathy. *Hepatology* 2008; 47: 596-604.
11. Venkaramarao SH, Mittal, Prabhakar S, Dhiman RK. Brain perfusion single photon emission computed tomography (SPECT) abnormalities in patients with minimal hepatic encephalopathy. *J Gastroenterol Hepatol* 2008; 23 : A62

12. Weissenborn K. Diagnosis of subclinical hepatic encephalopathy. *Med SciMonit* 1999;5: 568-575.
13. Romero-Gómez M, Córdoba J, Jover R et al. Value of the critical flicker frequency in patients with minimal hepatic encephalopathy. *Hepatology* 2007; 45: 879–85.
14. Amodio P, Del Piccolo F, Pettenò E et al. Prevalence and prognostic value of quantified electroencephalogram (EEG) alterations in cirrhotic patients. *J. Hepatol.* 2001; 35: 37–45.